PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
SJK/BP5254222		
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/GB 96/02405	30/09/1996	28/09/1995
Applicant		
MEDICAL RESEARCH COUNCIL et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. [X] **Certain claims were found unsearchable** (see Box I).

2. [ ] **Unity of invention is lacking** (see Box II).

3. [ ] The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
   - [ ] filed with the international application.
   - [ ] furnished by the applicant separately from the international application,
     - [ ] but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
   - [ ] Transcribed by this Authority

4. With regard to the **title,**
   - [X] the text is approved as submitted by the applicant.
   - [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**
   - [X] the text is approved as submitted by the applicant.
   - [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:
   Figure No. _____
   - [ ] as suggested by the applicant.
   - [ ] because the applicant failed to suggest a figure.
   - [ ] because this figure better characterizes the invention.
   - [X] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 96/ 02405

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claim(s) 24
is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 96/02405

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/86 C12N5/10 A61K35/76 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 00103 A (WISTAR INST ;UNIV PENNSYLVANIA (US)) 7 January 1993 see the whole document ---	1-24
X	WO 93 25234 A (UNIV CALIFORNIA) 23 December 1993 see the whole document ---	1-24
X	WO 94 27643 A (TARGETED GENETICS CORP ;PAUL RALPH W (US); OVERELL ROBERT (US)) 8 December 1994 see the whole document ---	1-24
X	WO 94 06920 A (MEDICAL RES COUNCIL ;RUSSELL STEPHEN JAMES (GB); HAWKINS ROBERT ED) 31 March 1994 see the whole document --- -/--	1-24

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

1

Date of the actual completion of the international search
6 February 1997

Date of mailing of the international search report
07.03.97

Name and mailing address of the ISA
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Authorized officer
Hillenbrand, G

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 96/02405

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 96 00294 A (MEDICAL RES COUNCIL ;RUSSELL STEPHEN JAMES (GB); COSSET FRANCOIS L) 4 January 1996 see the whole document ---	1-7, 9-14, 16-24
E	WO 96 33281 A (VIAGENE INC ;SYSTEMIX (US)) 24 October 1996 see the whole document -----	1-7, 9-14, 16-24

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

[illegible]nation on patent family members

[illegible]national Application No
[illegible]CT/GB 96/02405

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO-A-9300103	07-01-93	BR-A-	9300910	15-11-94
WO-A-9325234	23-12-93	EP-A-	0650370	03-05-95
		JP-T-	7507689	31-08-95
WO-A-9427643	08-12-94	AU-A-	7097494	20-12-94
WO-A-9406920	31-03-94	AU-A-	4827893	12-04-94
		CA-A-	2145063	31-03-94
		EP-A-	0670905	13-09-95
		JP-T-	8504091	07-05-96
WO-A-9600294	04-01-96	AU-A-	2749595	19-01-96
WO-A-9633281	24-10-96	AU-A-	5557196	07-11-96

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C12N 15/86, 5/10, A61K 35/76, 48/00 — A1

(11) International Publication Number: WO 97/12049

(43) International Publication Date: 3 April 1997 (03.04.97)

(21) International Application Number: PCT/GB96/02405

(22) International Filing Date: 30 September 1996 (30.09.96)

(30) Priority Data:
9519776.0 28 September 1995 (28.09.95) GB

(71) Applicant *(for all designated States except US)*: MEDICAL RESEARCH COUNCIL [GB/GB]; 20 Park Crescent, London W1N 4AL (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: RUSSELL, Stephen, James [GB/GB]; 10 Courtyards, Little Shelford, Cambridge CB2 5ER (GB). FIELDING, Adele, Kay [GB/GB]; Annex Flat, The Hall, Six Mile Bottom, Cambridge CB8 0UF (GB). CASIMIR, Colin, Maurice [GB/GB]; Imperial College School of Medicine at St Mary's, Norfolk Place, London W2 1PG (GB).

(74) Agents: KIDDLE, Simon, J. et al.; Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP (GB).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: MATERIALS AND METHODS RELATING TO THE TRANSFER OF NUCLEIC ACID INTO QUIESCENT CELLS

(57) Abstract

Materials and methods for transferring nucleic acid encoding a polypeptide for treating a disease or disorder into populations of quiescent cells such as haematopoietic stem cells (HSCs), using retroviral packaging cell lines and retroviral particles expressing and displaying a growth factor such as stem cell factor (SCF) on the cell surface or as a fusion with a viral envelope protein. The present invention also relates to compositions comprising the retroviral packaging cell lines and retroviral particles, and their use in methods of medical treatment, *in vivo* and *ex vivo*.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 96/02405

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/86 C12N5/10 A61K35/76 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 00103 A (WISTAR INST ;UNIV PENNSYLVANIA (US)) 7 January 1993 see the whole document ---	1-24
X	WO 93 25234 A (UNIV CALIFORNIA) 23 December 1993 see the whole document ---	1-24
X	WO 94 27643 A (TARGETED GENETICS CORP ;PAUL RALPH W (US); OVERELL ROBERT (US)) 8 December 1994 see the whole document ---	1-24
X	WO 94 06920 A (MEDICAL RES COUNCIL ;RUSSELL STEPHEN JAMES (GB); HAWKINS ROBERT ED) 31 March 1994 see the whole document --- -/--	1-24

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

1

Date of the actual completion of the international search
6 February 1997

Date of mailing of the international search report
07.03.97

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Authorized officer
Hillenbrand, G

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 96/02405

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 96 00294 A (MEDICAL RES COUNCIL ;RUSSELL STEPHEN JAMES (GB); COSSET FRANCOIS L) 4 January 1996 see the whole document ---	1-7, 9-14, 16-24
E	WO 96 33281 A (VIAGENE INC ;SYSTEMIX (US)) 24 October 1996 see the whole document -----	1-7, 9-14, 16-24

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 96/02405

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark: Although claim(s) 24 is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB 96/02405

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO-A-9300103	07-01-93	BR-A-	9300910	15-11-94
WO-A-9325234	23-12-93	EP-A-	0650370	03-05-95
		JP-T-	7507689	31-08-95
WO-A-9427643	08-12-94	AU-A-	7097494	20-12-94
WO-A-9406920	31-03-94	AU-A-	4827893	12-04-94
		CA-A-	2145063	31-03-94
		EP-A-	0670905	13-09-95
		JP-T-	8504091	07-05-96
WO-A-9600294	04-01-96	AU-A-	2749595	19-01-96
WO-A-9633281	24-10-96	AU-A-	5557196	07-11-96

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PATENT COOPERATION TREATY

PCT

REC'D 12 JAN 1998
WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
SJK/BP5254222		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB 96/ 02405	30/09/1996	28/09/1995
International Patent Classification (IPC) or national classification and IPC		
C12N15/86		
Applicant		
MEDICAL RESEARCH COUNCIL et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consists of a total of 4 sheets.

3. This report contains indications and corresponding pages relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23/04/1997	08.05.98
Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	G. Hillenbrand Telephone No. 8428

Intern. application No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

PCT/GB96/02405

I. Basis of the report

1. This report has been drawn up on the basis of (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

[ ] the international application as originally filed.

[x] the description, pages 1-30, as originally filed,
pages _____, filed with the demand,
pages _____, filed with the letter of _____,
pages _____, filed with the letter of _____,

[x] the claims, Nos. _____, as originally filed,
Nos. _____, as amended under Article 19,
Nos. _____, filed with the demand,
Nos. 1-21, filed with the letter of 17.09.97,
Nos. _____, filed with the letter of _____,

[x] the drawings, sheets/fig 1-9, as originally filed,
sheets/fig _____, filed with the demand,
sheets/fig _____, filed with the letter of _____,
sheets/fig _____, filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

[ ] the description, pages _____.
[ ] the claims, Nos. _____.
[ ] the drawings, sheets/fig _____.

3. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 3,15	YES
	Claims 1-2,4-14,16-21	NO
Inventive Step (IS)	Claims	YES
	Claims 3,15	NO
Industrial Applicability (IA)	Claims 1-21	YES
	Claims	NO

2. CITATIONS AND EXPLANATIONS

Document (1) : WO-A-93/00103
Document (2) : WO-A-94/27643
Document (3) : WO-A-94/06920

1. Having regard to documents (1) - (3) cited in the International Search Report, the subject-matter of Claims 1-2, 4-14 and 16-21 lacks novelty (Article 33.2 PCT).

As admitted by the applicant on page 2 of the application the production of quiescent cells is known to the skilled person.

D1 describes already a method of transforming such quiescent cells ((pluripotent) stem cells) using as ligand GM-CSF which binds to the GM-CSF receptor of stem cells. This embodiment permits the delivery of effectors (such as genes) to the pluripotent stem cells to correct blood-born disorders disorders (see page 23, lines 5-15 and claim 8). Thus, the subject-matter of at least Claims 1, 5, 9-11, 13, 17 and 19 lacks novelty in view

of D1.

D2 also discloses a method of transforming quiescent cells (hemotopoietic stem cells - HSCs), which HSCs are explicitly mentioned on page 39 of the description. Neither any problems concerning the production of hemotopoietic stem cells, nor problems concerning the transformation of these cells are reported on page 39 of D2. Thus, it is not visible how the very broadly and imprecisely worded subject-matter of Claims 1-2, 4-14 and 16-21 could differ from D2.

Finally D3 deals in great detail with the genetic modification of HSCs by direct in vivo gene transfer using recombinant retroviruses (see the description pages 29-31, page 40, point 10 and page 56, paragraph 2). Again, it is not visible by which defined technical features the broadly drafted matter of Claims 1-2, 4-14 and 16-21 differentiates from the content of D3.

2. The subject-matter of Claims 3 and 15 is considered to be novel but lacks the required inventive step (Article 33.3 PCT). In view of the documents cited above the use of SCF or FLT3-ligand as growth factor must be considered as obvious modification of the known retroviral packaging cell lines, which does not require any inventive activity.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO-A-96/00294	04.01.96	27.06.95	27.06.94
WO-A-96/33281	24.10.96	19.04.96	20.04.95

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The applicant is informed that in the present case the reply of the applicant dated 17/09/97 received the office on 22/09/07. The deadline for the submission of a second 408 expired only a view days later on 28/09/97. Due to the heavy workload of the IPE Authority, the submission of a further 408 within this short time span was not possible. Thus we regret that no further opportunity to submit further amendments or arguments could be given to the applicant.

Replaced by Article 34 Amendment.

CLAIMS:

1. A retroviral packaging cell line transformed with a viral vector comprising nucleic acid encoding a polypeptide for treating a disease or disorder, the retroviral packaging cell line being capable of expressing nucleic acid encoding a growth factor so that the growth factor is (i) displayed on the cell surface or (ii) expressed as a fusion with a viral envelope protein so that the growth factor is displayed on the surface of viral particles,

wherein the cell line packages the nucleic acid encoding the polypeptide in viral particles produced by the retroviral packaging cell line, the cell line being for use in a method of medical treatment of a disease or disorder that responds to the polypeptide.

2. The retroviral packaging cell line of claim 1 wherein the medical treatment is transfer of the nucleic acid encoding the polypeptide to a population of quiescent cells which are induced to divide by the surface bound growth factor, so that the nucleic acid is incorporated into the genome of the quiescent cells.

3. The retroviral packaging cell line of claim 1 or claim 2 wherein the cells are haematopoeitic stem cells.

4. The retroviral packaging cell line of any one of claims 1 to 3 wherein growth factor is stem cell factor or FLT3 ligand.

5. The retroviral packaging cell line of claim 4 wherein growth factor is stem cell factor.

6. The retroviral packaging cell line of any one of the preceding claims further expressing nucleic acid encoding a receptor to target the cells to the bone marrow and/or an immunosuppressive factor so that the receptor and/or

Replaced by Article 34 Amendment

immunosuppressive factor are displayed on the cell surface.

7. Retroviral particles displaying a surface bound growth factor as a fusion with an envelope protein, the particles being produced by the retroviral packaging cell line of any one of the preceding claims.

8. The retroviral particle of claim 7 wherein the growth factor is SCF or FLT3-ligand.

9. The retroviral particles of claim 7 or claim 8 wherein the growth factor is attached to the N-terminus of a retroviral envelope protein.

10. The retroviral particle of any one of claims 7 to 9 wherein envelope protein is viral envelope SU protein.

11. The retroviral particle of any one of claims 7 to 10 wherein the growth factor is fused to the envelope protein via a cleavable linker.

12. The retroviral particles of any one of claims 7 to 11 wherein the particle displays multiple growth factors.

13. A composition comprising a retroviral packaging cell line or retroviral particles of any one of claims 1 to 12, in combination with a suitable carrier.

14. A retroviral packaging cell line expressing nucleic acid encoding a growth factor as a fusion with an envelope glycoprotein so that the growth factor is displayed on the surface of the cell line.

15. The retroviral packaging cell line of claim 14 wherein the growth factor is FLT3-ligand.

16. The retroviral packaging cell line of claim 14 or

claim 15 wherein the cell line is a lentiviral packaging cell line.

17. The use of a retroviral cell line or retroviral particles of any one of claims 1 to 12 in the preparation of a medicament for treating a disease or disorder that responds to the polypeptide encoded by the nucleic acid packaged in the retroviral particles.

18. The use of claim 17 wherein the medicament comprising the retroviral packaging cell line or retroviral particles is administered by implantation into a patient's bone marrow or by infusion into a patient's blood.

19. The use of claim 18 wherein the retroviral packaging cell line expresses a receptor to target the cells to the bone marrow and/or an immunosuppressive factor on their surface.

20. A method of transforming a population of quiescent cells with nucleic acid encoding a polypeptide so that the nucleic acid is incorporated into the genome of the cells, the method comprising exposing the cells to a retroviral packaging cell line or retroviral particles of any one of claim 1 to 12, wherein the surface bound growth factor induces the cells to divide, so that the nucleic acid encoding the polypetide for treating a disease or disorder contained in the viral particles can incorporate into the genome of the cells.

21. The method of claim 20 wherein the quiescent cells are a population of bone marrow cells enriched in haematopoeitic stem cells.

22. A population of cells produced by the method of claim 20 or claim 21 having the nucleic acid encoding a polypeptide for treating a disease or disorder stably

Replaced by Article 34 Amendment

incorporated into their genome.

23. A pharmaceutical composition comprising the cells of claim 22.

24. A method for introducing nucleic acid encoding a polypeptide for treating a disease or disorder into the genome of a population of cells *in vivo*, the method comprising adminstering a retroviral packaging cell line or retroviral particles of any one of claims 1 to 12 by implantation into a patient's bone marrow or by infusion into a patient's blood.